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cont expression of the heterologous protein is regulated in a tissue specific manner.

REMARKS

This submission is in response to the Official Action dated January 14, 2003. Claims 28, 33, 38 and 39 have been amended. Claims 29 and 34 have been allowed. Claims 28-39 are currently pending.

Claims 28 and 33 have been amended to recite that the level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor results in an increase (claim 28) or a decrease (claim 33) in the level of β_3-AR gene product. Support for this amendment can be found throughout the specification and in particular on page 27 lines 4-9 and page 29 line 5 - page 30 line 3.

Claims 38 and 39 have been amended to provide antecedent basis for the phrases in sections (iii) and (iv) of the claims objected to by the Examiner.

No new matter has been added by these amendments. Reconsideration of the above identified application, in view of the above amendments and the following remarks, is respectfully requested.

REJECTIONS UNDER 35 USC § 112, FIRST PARAGRAPH

Claim 28 (and its dependent claims 31 and 32) and claim 33 (and its dependent claims 36 and 37) have been rejected for alleged failure to fulfill the

written description requirement. Specifically, the Examiner alleges that the phrase "in a level of activity" encompasses literally any activity that may be associated with Sp1 or B segment-binding β_3-adrenergic receptor trans-activating factors and that the specification only describes these activities in relation to expression of the β_3-adrenergic receptor gene. The Examiner has indicated that this rejection would be overcome if the detection of activity was linked to β_3-adrenergic receptor gene expression.

As recommended by the Examiner, claims 28 and 33 have been amended to recite that the level of activity results in an increase (or decrease) in the level of β_3-AR gene product. These amendments do not narrow the scope of the claims. It is believed that the rejections of claims 28 and 33 have been obviated and Applicants respectfully request that these rejections be withdrawn.

REJECTIONS UNDER 35 USC §112, SECOND PARAGRAPH

Claims 30 and 35 have been rejected as indefinite because the end result of the claim allegedly does not necessarily match the preamble of the claim. Specifically, the Examiner contends that the amount of the transcription factor does not necessarily correlate to the level of activity of the transcription factor.

Applicants respectfully disagree. The art generally recognizes a correlation between the amount of transcription factor and its activity. The

correlation between amount of transcription factor and its activity is the principle behind assays standard in the field such as gel shift assays. In addition, assays to detect the amount of Sp1 or B segment-binding β_3-AR *trans*-activating factor associated with nucleic acid containing the B segment core binding sequence are described in the specification as assays appropriate for screening for compounds that increase or decrease the activity of β_3-AR trans-activating factors (see e.g. page 30 lines 9-17). Accordingly, Applicants respectfully request withdrawal of this rejection.

The Examiner has rejected claim 31 as indefinite. Specifically, the Examiner contends that the term "express at a very low level, β_3-AR" is not defined clearly in the specification.

Applicants respectfully disagree. Page 29 lines 11-18 of the specification gives several examples of cells that express β_3-AR at very low levels (WAT cells, muscle cells, liver cells, HeLa and CV-1 cells) and explains that the level of expression of β_3-AR in these cells is very low *relative* to β_3-AR-expressing cells. The phrase "relative to β_3-AR-expressing cells" defines what "very low levels" means by relating the level to specific levels known in the art (e.g. the level expressed in WAT, muscle, liver, HeLa and CV-1 cells).

The specification also discloses other examples of cells that express β_3-AR at low levels. For example, page 5 lines 11-13 of the specification states

that β_3-AR is expressed by mouse brown adipose tissue cells, but is expressed at very low levels by human white adipocytes. See also page 51 lines 25-28 of the specification. The specification also points to two references (Wilson *et al.*, The Journal of Pharmacology and Experimental Therapeutics 279:214-221, 1996, cited on page 3 lines 19-20 of the specification and Strosberg, Annu. Rev. Pharmacol. Toxicol., 37:421-450, 1997, cited on page 51 lines 23-24 of the specification) that demonstrate low levels of β_3-AR expression. Thus, one skilled in the art could readily determine low levels of β_3-AR expression and could also readily identify cells that "express at a very low level, β_3-AR." Accordingly, Applicants believe this rejection has been overcome and respectfully request that this rejection be withdrawn.

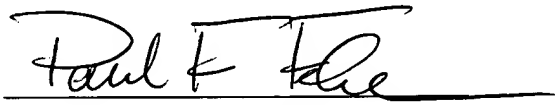
The Examiner has also rejected claims 38 and 39 for alleged indefiniteness because of an alleged lack of antecedent basis for the phrases "the sequence that is greater than 80% identical to the nucleotide sequence" and "the Sp1-binding site." Claims 38 and 39 have been amended to provide antecedent basis for these phrases. Thus, this rejection has been obviated and Applicants respectfully request withdrawal of this rejection.

CONCLUSION

Therefore, in view of the above amendments and remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue.

If there are any other issues remaining which the Examiner believes could be resolved through either a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

Respectfully submitted,



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Docket No: 0630/1E791-US1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Vedrana S. SUSULIC; Emir DUZIC

Serial No.: 09/761,116 Art Unit: 1636

Confirmation No.: 3094

Filed: January 16, 2001 Examiner: Leffers Jr., Gerald

For: TRANSCRIPTIONAL REGULATION OF THE HUMAN BETA3 - ADRENERGIC RECEPTOR GENE

MARK-UP AMENDMENT

Hon. Commissioner of
Patents and Trademarks
Washington, DC 20231

April 14, 2003

Sir:

28. (Twice Amended) A method of screening for a compound that

increases activity of an Sp1 or B segment-binding β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the Sp1 or B segment-binding β_3-AR *trans*-activating factor with a test compound; and

(b) detecting an increase in a level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor,

wherein the increase in the level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor results in an increase in the level of β_3-AR gene product relative to a level of expression prior to contact with the test compound.

33. (Twice Amended) A method of screening for a compound that inhibits activity of an Sp1 or B segment-binding β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the Sp1 or B segment-binding β_3-AR *trans*-activating factor with a test compound; and

(b) detecting a decrease in a level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor,

wherein the decrease in the level of activity of the Sp1 or B segment-binding β_3-AR *trans*-activating factor results in a decrease in the level of β_3-AR gene product relative to a level of expression prior to contact with the test compound.

38. (Amended) A method of screening for a compound that increases activity of a β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the β_3-AR *trans*-activating factor with a test compound; and

(b) detecting an increase in a level of activity of the β_3-AR *trans*-activating factor,

wherein the level of activity of the β_3-AR *trans*-activating factor is detected by an increase in the level of expression of a reporter gene operatively associated with an isolated nucleic acid selected from the group consisting of:

(i) about a 7 kb genomic DNA 5' flanking region of a β_3-AR transcription start site,

(ii) a deletion construct of a 7 kb genomic DNA located upstream of a β_3-AR transcription start site;

(iii) a nucleic acid [wherein the] <u>comprising a nucleotide</u> sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) [is] located 5' to [the] <u>an</u> Sp-1 binding site relative to a transcription start site; and

(iv) a nucleic acid comprising a heterologous coding sequence

operatively associated with a promoter and operatively associated with [the] a nucleotide sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) in proximity to [the] an Sp-1 binding site, whereby expression of the heterologous protein is regulated in a tissue specific manner.

39. (Amended) A method of screening for a compound that decreases activity of a β_3-adrenergic receptor (β_3-AR) *trans*-activating factor in human cells, which method comprises:

(a) contacting cells capable of producing the β_3-AR *trans*-activating factor with a test compound; and

(b) detecting [an] a decrease in a level of activity of the β_3-AR *trans*-activating factor, wherein the level of activity of the β_3-AR *trans*-activating factor is detected by [an] a decrease in the level of expression of a reporter gene operatively associated with an isolated nucleic acid selected from the group consisting of:

(i) about a 7 kb genomic DNA 5' flanking region of a β_3-AR transcription start site,

(ii) a deletion construct of a 7 kb genomic DNA located upstream of a β_3-AR transcription start site;

(iii) a nucleic acid [wherein the] comprising a nucleotide sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) [is] located 5' to [the] an Sp-1 binding site relative to a transcription start site; and

(iv) a nucleic acid comprising a heterologous coding sequence operatively associated with a promoter and operatively associated with [the] a nucleotide sequence that is greater than 80% identical to the nucleotide sequence GCCTCTGGGGAG (SEQ ID NO:1) in proximity to [the] an Sp-1 binding site, whereby expression of the heterologous protein is regulated in a tissue specific manner.